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Piracetam for fetal distress in labour (Review)

Hofmeyr GJ, Kulier R

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TABLE OF CONTENTS

[Intervention Review]

Piracetam for fetal distress in labour

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ABSTRACT

Background

Piracetam is thought to promote the metabolism of brain cells when they are hypoxic. It has been used to prevent adverse effects of fetal distress.

Objectives

The objective of this review was to assess the effects of piracetam for suspected fetal distress in labour on method of delivery and perinatal morbidity.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (15 February 2012).

Selection criteria

Randomised trials of piracetam compared with placebo or no treatment for suspected fetal distress in labour.

Data collection and analysis

Both review authors assessed eligibility and trial quality.

Main results

One study of 96 women was included. Piracetam compared with placebo was associated with a trend to reduced need for caesarean section (risk ratio 0.57, 95% confidence interval 0.32 to 1.03). There were no statistically significant differences between the piracetam and placebo group for neonatal morbidity (measured by neonatal respiratory distress) or Apgar score.

Authors' conclusions

There is not enough evidence to evaluate the use of piracetam for fetal distress in labour.

PLAIN LANGUAGE SUMMARY

Piracetam for fetal distress in labour

Piracetam is thought to support the metabolism of brain cells when they have an insufficient oxygen supply (hypoxia). It may, therefore, prevent any adverse effects for an infant with persistent fetal distress during labour.

This review set out to assess the effects of piracetam for suspected fetal distress in labour on method of delivery and newborn ill effects (morbidity). Only one controlled trial was identified. The trial randomised 96 women to receive either piracetam or a placebo. Piracetam treatment was associated with a trend toward reduced need for a caesarean section as the method of delivery and an improved outcome for the newborn as determined by respiratory problems and signs of hypoxia. The trial did not provide information about any side effects experienced by the mother. This evidence is insufficient for meaningful conclusions.

BACKGROUND

Piracetam, a derivative of gamma-aminobenzoic acid, is thought to promote the metabolism of the brain cells when they are hypoxic. It has therefore, been considered as a possible intervention for ameliorating the effects of perinatal asphyxia (Margaria Mutani 1974). Its use in persistent intrapartum fetal distress to 'treat' the fetus to prevent any adverse effects has been evaluated in a single placebo-controlled trial (Huaman 1983).

For further information *see* Grant 1989.

OBJECTIVES

To determine, from the best available evidence, the effects on method of delivery and perinatal morbidity of piracetam treatment for suspected fetal distress in labour.

METHODS

Criteria for considering studies for this review

Types of studies

Clinical trials comparing effects of piracetam treatment for suspected fetal distress in labour with placebo or no treatment; random allocation to treatment and control groups, with adequate allocation concealment; violations of allocated management and exclusions after allocation not sufficient to materially affect outcomes.

Types of participants

Women with suspected fetal distress in labour.

Types of interventions

Piracetam versus placebo or no treatment.

Types of outcome measures

Method of delivery; measures of perinatal morbidity and mortality; side effects for women.
Outcomes included if clinically meaningful; reasonable measures taken to minimise observer bias; missing data insufficient to materially influence conclusions; data available for analysis according to original allocation, irrespective of protocol violations; data available in format suitable for analysis.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (15 February 2012).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. weekly searches of EMBASE;
4. handsearches of 30 journals and the proceedings of major conferences;
5. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL, MEDLINE and EMBASE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

We did not apply any language restrictions.

Data collection and analysis

The trial under consideration was evaluated for methodological quality and appropriateness for inclusion according to the prestated selection criteria, without consideration of the results. Individual outcome data were included in the analysis if they met the prestated criteria in 'Types of outcome measures'. Included trial data were processed as described in Clarke 2000.

Data were extracted from the source and entered onto the Review Manager (RevMan) computer software (RevMan 2000), checked for accuracy, and analysed as above using the RevMan software. For dichotomous data, risk ratios and 95% confidence intervals were calculated.

RESULTS

Description of studies

See table of 'Characteristics of included studies'.

Risk of bias in included studies

See table of 'Characteristics of included studies', particularly the 'Methods' and 'Notes' sections.

In the double-blind placebo-controlled study of Huaman et al (Huaman 1983), some selection bias may have been introduced by the exclusion of two participants who delivered shortly after enrolment and two with infection-related fetal malformations, but the number excluded is relatively small in relation to the 96 women studied. Whether or not the subjective outcomes such as Apgar score and neurological examination were recorded blind to the allocation of each baby is not specified.

Effects of interventions

Piracetam treatment was associated with a trend to reduced need for caesarean section (risk ratio (RR) 0.57, 95% confidence interval (CI) 0.32 to 1.03), and improved neonatal outcome as judged by neonatal respiratory problems and signs of hypoxia (RR 0.09, 95% CI 0.01 to 1.60). The Apgar score results are consistent with anything from a large beneficial to a small adverse effect. No information is available on maternal side effects.

DISCUSSION

Only one trial has been reviewed, and the evidence is insufficient for meaningful conclusions.

AUTHORS' CONCLUSIONS

Implications for practice

There is insufficient evidence to support the use of piracetam for fetal distress in labour.

Implications for research

Because only one randomized trial of piracetam for fetal distress has, to our knowledge, been reported, there is scope for further trials of this intervention.

ACKNOWLEDGEMENTS

None.

REFERENCES

References to studies included in this review

Huaman 1983 *{published data only}*

Huaman EJ, Hassoun R, Itahashi CM, Pereda GJ, Mejia MA. Results obtained with piracetam in foetal distress during labour. *Journal of International Medical Research* 1983;**11**:129-36.

References to studies excluded from this review

Klink 1979 *{published data only}*

Klink F, Grosspietzsch R, von Klitzing L, Oberheuser F. [The protective effect of piracetam during delivery] [Zur protektiven wirkung von piracetam unter der geburt]. *Fortschritte der Medizin* 1979;**97**:2163-5.

Additional references

Clarke 2000

Clarke M, Oxman AD, editors. Cochrane Reviewers' Handbook 4.1 [updated July 2000]. In: Review Manager (RevMan) [Computer program]. Version 4.1. Oxford, England: The Cochrane Collaboration, 2000.

Grant 1989

Grant AM. Monitoring the fetus during labour. In: Chalmers I, Enkin MW, Keirse MJNC editor(s). Effective care in pregnancy and childbirth. Oxford: Oxford University Press, 1989:846-82.

Margaria Mutani 1974

Margaria Mutani E. Preliminary experimental and clinical trials of prevention and therapy of perinatal distress with piracetam. *Anesthesie, Analgesie, Reanimation* 1974;**3**:397-408.

RevMan 2000 [Computer program]

The Cochrane Collaboration. Review Manager (RevMan). Version 4.1 for Windows. Oxford, England: The Cochrane Collaboration, 2000.

References to other published versions of this review

Hofmeyr 1995

Hofmeyr GJ. Piracetam for fetal distress in labour. [revised 24 March 1993]. In: Enkin MW, Keirse MJNC, Renfrew MJ, Neilson JP, Crowther C (eds.) Pregnancy and Childbirth Module. In: The Cochrane Pregnancy and Childbirth Database [database on disk and CDROM]. The Cochrane Collaboration; Issue 2, Oxford: Update Software; 1995.

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Huaman 1983

Methods	Double-blind placebo- controlled randomised study.
Participants	Women with diagnosis of acute fetal distress (meconium stained amniotic fluid and/or pathological fetal heart rate pattern).
Interventions	Piracetam (n = 48) versus placebo (n = 48), intravenously 6 ampoules at once and 2 ampoules hourly.
Outcomes	Time to delivery; Apgar scores; morbidity on clinical and neurological assessment at 24 hours (respiratory difficulties, signs of slight to severe hypoxia); placental histology.
Notes	Lima, Peru. Some selection bias may have been introduced by the exclusion of 2 participants who delivered shortly after enrolment and 2 with infection-related fetal malformations, but the number excluded is relatively small in relation to the number studied. Whether or not the subjective outcomes such as Apgar score and neurological examination were recorded blind to the allocation of each baby is not specified.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	Adequate

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Klink 1979	Excluded because healthy fetuses were studied, not compromised fetuses. Piracetam was administered to 17 nulliparous women during labour (10 g i.v./h), and placebo to 9 women. Following piracetam, fetal EEG showed an activation of alpha-waves with reduction of delta-waves, CTG showed reduced decelerations during the expulsion period and Apgar scores were better than 9 in all cases.

CTG: cardiotocograph
EEG: electroencephalography
i.v.: intravenous

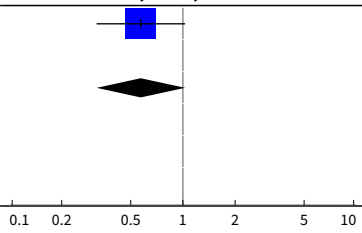
DATA AND ANALYSES

Comparison 1. Piracetam for fetal distress in labour

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Caesarean section	1	96	Risk Ratio (M-H, Fixed, 95% CI)	0.57 [0.32, 1.03]
2 Apgar score < 7 at 1 minute	1	96	Risk Ratio (M-H, Fixed, 95% CI)	0.4 [0.08, 1.96]
3 Neonatal morbidity	1	96	Risk Ratio (M-H, Fixed, 95% CI)	0.09 [0.01, 1.60]

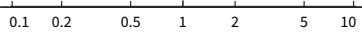
Analysis 1.1. Comparison 1 Piracetam for fetal distress in labour, Outcome 1 Caesarean section.

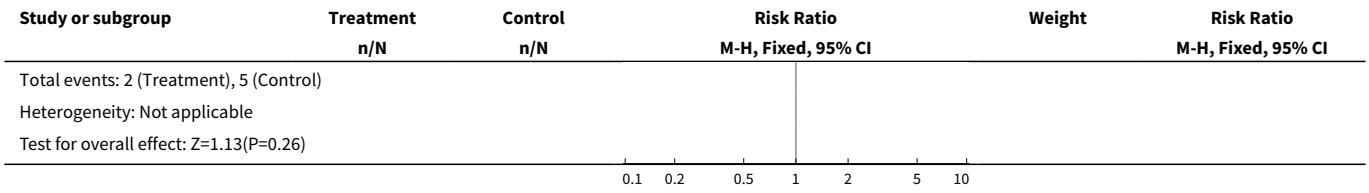
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Huaman 1983	12/48	21/48		100%	0.57[0.32,1.03]
Total (95% CI)	**48**	**48**		**100%**	**0.57[0.32,1.03]**
Total events: 12 (Treatment), 21 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.87(P=0.06)					



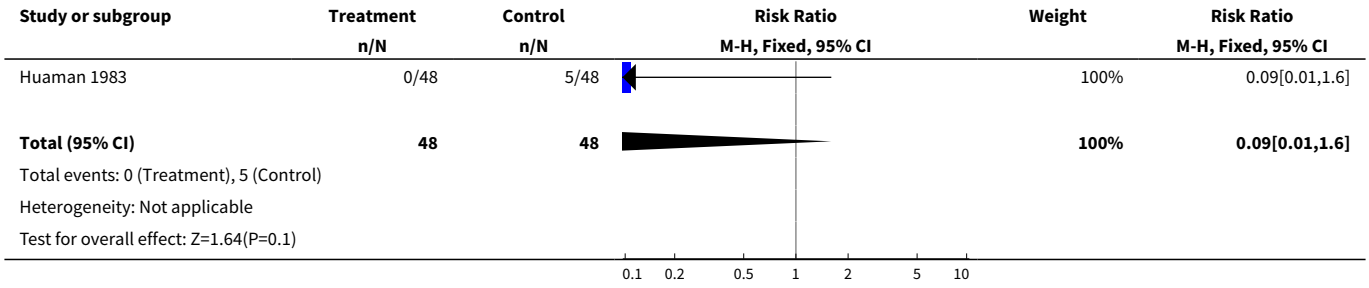
Analysis 1.2. Comparison 1 Piracetam for fetal distress in labour, Outcome 2 Apgar score < 7 at 1 minute.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Huaman 1983	2/48	5/48		100%	0.4[0.08,1.96]
Total (95% CI)	**48**	**48**		**100%**	**0.4[0.08,1.96]**





Analysis 1.3. Comparison 1 Piracetam for fetal distress in labour, Outcome 3 Neonatal morbidity.



WHAT'S NEW

Date	Event	Description
17 February 2012	New citation required but conclusions have not changed	Review updated.
17 February 2012	New search has been performed	Search updated. No new trials identified.

HISTORY

Protocol first published: Issue 2, 1998
Review first published: Issue 2, 1998

Date	Event	Description
2 July 2010	Amended	Contact details edited.
24 June 2009	New search has been performed	Search updated. No new trials identified. Plain language summary added.
20 September 2008	Amended	Converted to new review format.
25 October 2004	New search has been performed	Search updated. No new trials identified.
30 September 2001	New search has been performed	One study (Klink 1979) was evaluated and not included in the review.

CONTRIBUTIONS OF AUTHORS

GJ Hofmeyr prepared the original version, and is responsible for maintaining the review. R Kulier quality-checked and revised the review.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- University of the Witwatersrand, South Africa.
- Department of Obstetrics and Gynaecology, Geneva University Hospital, Switzerland.

External sources

- South African Medical Research Council, South Africa.
- The Nuffield Trust, UK.

INDEX TERMS

Medical Subject Headings (MeSH)

*Labor, Obstetric; Apgar Score; Cesarean Section [statistics & numerical data]; Delivery, Obstetric; Fetal Distress [*drug therapy]; Neuroprotective Agents [*therapeutic use]; Piracetam [*therapeutic use]; Randomized Controlled Trials as Topic

MeSH check words

Female; Humans; Pregnancy